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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/367,013	08/05/1999	DEBORAH KNUTZON	86014/8145	3773

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EXAMINER	
NASHED, NASHAAT T	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 11/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/367,013	KNUTZON ET AL.	
	Examiner	Art Unit	
	Nashaat T. Nashed, Ph. D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *215-244,255-274 and 298-373* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *215-224,255-264,325,328,338,341,351,354,364 and 367* is/are allowed.

6)☐ Claim(s) *225-244, 265-274, 298-322, 326, 327, 329-335, 339, 340, 342-348, 352, 353, 356-361, 365, 366, and 368-372* is/are rejected.

7)☒ Claim(s) *323,324,336,337,349,350,362,363 and 373* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/7/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 7, 2005 has been entered.

The application has been amended as requested in the communication filed August 19, 2005. Accordingly, claims 219-223 have been amended, claims 245 and 246 have been entered, and claims 199, 218, and 236-240 have been canceled as requested.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 235-244, 327, 340, 353, and 366 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 235-244, 327, 340, 353, and 366 are directed to methods of using a transformed microbial cell comprising any deletion mutation of one or more nucleotide of SEQ ID NO: 1. The specification, however, does not even provide a single representative species of the deletion mutants of SEQ ID NO: 1 encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship. No teaching of the catalytic amino acid residues of SEQ ID NO: 2 or the various amino acid residues which can be deleted without affecting the function of the protein of SEQ ID NO: 2. Given this lack of additional representative species as encompassed by the claims and identify a structural activity relationship, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 298, 299, 301-309, 330, 343, 356, and 369 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The phrase "under hybridization condition suitable for selectively screening a recombinant DNA library" does not appear any where in the specification and the original claims. Applicants alleged that the claim could find its support in example 1 and 2. The examiner could not find any. Thus, the phrase constitutes a new matter, which should be deleted.

Claims 300, 310-318, 331, 344, 357, and 370 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 300, 310-318, 331, 344, 357, and 370 are directed to any a method of making oil with increases levels of polyunsaturated fatty acid using a plant transformed with any nucleic acid encoding a 6-desaturase activity from *Mortierella alpina*. The specification, however, only provides a single representative species from *Mortierella alpina* having the amino acid sequence of SEQ ID NO: 2 encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these DNAs by any identifying structural characteristics or properties other than the activities recited in claims 300, 310-318, 331, 344, 357, and 370, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 225-234, 265-274, 319-322, 326,329, 332-335, 339, 342, 345-348, 352, 355, 358-361, 365, 368, 371, and 372 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to methods of producing oil in stearidonic acid using microorganism transformed with the nucleic acid sequences having 95% sequence homology to SEQ ID NO: 1, or encoding a polypeptide having 95% sequence homology to SEQ ID NO: 2 including SEQ ID NO: 1 from *Mortierella alpina* for the reasons set forth in the prior Office actions mailed 10/21/01, 6/28/02, 12/31/02, and 10/6/03. The disclosure is enabling only for claims limited to methods of producing oil enriched in stearidonic acid using microorganism transformed with the nucleic acid sequences encoding Δ-6-desaturase of SEQ ID NO: 2 and Δ-12-desaturase of SEQ ID NO: 4 from *M. alpina*. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to all possible nucleic acid sequences which have 60%, 80% or 90% sequence homology to SEQ ID NO: 1, encoding an amino acid sequence that is 60%, 80%, or 90% homologues to SEQ ID NO: 2, or having any number of deletion of SEQ

ID NO: 1, or hybridizes under any condition to the nucleic acid sequence of SEQ ID NO: 1. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses a general method of producing oil enriched with unsaturated fatty acid using a microbial cell transformed with any nucleic acid sequences which has 60%, 80% or 90% sequence homology to SEQ ID NO: 1, encoding an amino acid sequence which is 60%, 80% or 90% homologues to SEQ ID NO: 2, having any number of deletion of SEQ ID NO: 1, or any nucleic acid sequence from any biological source that hybridizes under any conditions to the nucleic acid sequence of SEQ ID NO: 1. The specification provides guidance and examples in the form of an assay to isolate and characterize the nucleic acid encoding Δ-6-desaturase of SEQ ID NO: 2 and Δ-12-desaturase of SEQ ID NO: 4 from *M. alpina* and their use in producing oil with enriched in unsaturated fatty acid from a culture of microorganism (see examples 1-8) and isolation and determining the amount of each unsaturated fatty acid in an oil fraction. While molecular biological techniques and genetic manipulation to make the transformed microbial cell are known in the prior art and the skill of the artisan are well developed, knowledge regarding the redesigning of 40%, 20%, or 10% of the amino acid residues of the polypeptide of SEQ ID NO: 2 (91 amino acid residues) by deletion, insertion, substitution or combination thereof, while maintaining the Δ-6-desaturase activity, or identifying a nucleic acid sequence encoding a Δ-6-desaturase having 60%, 80% or 90% sequence homology to SEQ ID NO: 2 from any biological source is lacking. Thus, searching for a nucleic acid sequence having 60%, 80% or 90% homology to SEQ ID NO: 1, or encoding a polypeptide having 60%, 80% or 90% sequence homology to the amino acid sequence of SEQ ID NO: 1 is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation to identify a nucleic acid having 60%, 80%, or 90% sequence homology to SEQ ID NO: 1, encoding a Δ-6-desaturase polypeptide having 60%, 80% or 90% sequence homology toe SEQ ID NO: 2, having any number of deletion mutation of SEQ ID NO: 1, or hybridizes under any conditions to SEQ ID NO: 1 is enormous. Since routine experimentation in the art does not include screening vast numbers of genomic, cDNA or manmade DNA libraries, identifying a function of a protein product encoded by a nucleic acid isolated from said libraries, and develop a method to desaturate fatty acids between C6 and C7, where the expectation of obtaining the desired nucleic acid to utilize in the claimed method is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the biological source of the nucleic acid, the nucleic acid

sequences of other Δ-6-desaturase polypeptide, the three dimension structure of the polypeptide of SEQ ID NO: 2, and the amino acid residues which can be inserted, deleted, substituted without adverse effect on the folding of the polypeptide into a functional desaturase. Without such guidance, the experimentation left to those skilled in the art is undue.

In response to the above rejections, applicants argue that they are the first to disclose the *M. alpina* 6-desaturase DNA and protein and the first to characterize the activity of the encoded protein, and advised the Examiner to review the Board of Patent Appeal and Interference decision, Appeal No. 2004-2319 in application 09/915,694. Also, they argue that the claims at issues recite biological molecules having a reasonable relationship to the disclosed invention, and applicants in chemical and polymeric arts routinely obtain claims of enormous scope. They further argue that they have taught techniques that enable the full scope of the claimed invention. Finally, applicants argue that without evidence, and without an analysis of all the Wand factors for each claim, no *prima facie* case of non-enablement has been established.

Applicants' arguments filed 10/7/05 have been fully considered but they are not deemed to be persuasive. The examiner has restated the enablement rejection against the claims for the convenience of the applicants. Enablement requires a disclosure sufficient to allow a person of skill in the art to practice the full scope of the claimed invention without undue experimentation. The previous Office actions set out a *prima facie* case of non-enablement, explaining by sound scientific reasoning why a person of ordinary skill in the art would doubt that the guidance of the specification would enable practice of the full scope of the claimed invention without undue experimentation. The examiner has provided sufficient analysis of the Wand factors as they relate to the claimed invention. Applicants have presented no evidence or, indeed, any arguments to establish the adequacy of the disclosure to enable the scope of the instant claims. Applicants merely assert that they are the first to characterize the nucleic acid and polypeptide of the invention and they are entitled for a reasonable scope. The examiner in agreement that the applicants are entitled for a reasonable scope of the claimed invention, but what is reasonable is related to the prior art and the abilities of one of ordinary skill in the art in addition to the teaching of the specification. The amino acid sequence of SEQ ID NO: 2 is 457 amino acid residues. While random mutagenesis may produce mutants wherein less than a handful of amino acid residues have been substituted or deleted, no mutation or protein reengineering method known in the art or disclosed in the specification would enable one of ordinary skill in the art to substitute, delete, insert or combination thereof mutants of up to 91 and 183 amino acid residues (corresponding to 20% and 40%) of SEQ ID NO: 2. Claims 225-234, 265-274, 319-322, 326,329, 332-335, 339, 342, 345-348, 352, 355, 358-361, 365, 368, 371, and 372 are directed to a method of using microbial cells comprising nucleic acid encoding a polypeptide having 60%, 80% or 90% sequence homology to SEQ ID NO: 1 or 2. Thus,

the scope of the claimed invention is not reasonable because it is not commensurate in scope to teaching of the specification. This examiner is not aware of any wavers for the enablement requirement under 35 USC 112, first paragraph, for applicants who first to invent. If applicants are aware of any waver under 35 USC 112, first paragraph, for applicants who first to invent, they should bring it to the examiner's attention. The examiner will be happy to reconsider his position at that time. With regard to assertion that applicants in chemical and polymeric arts routinely obtain claims of enormous scope, the examiner is not aware of such a practice or rules that make the applicants are entitled for enormous scope. The enabled scope must meet the requirement of 35 USC 112, first paragraph and the teaching of the court *in re Wand*, which the instant claims failed to do so. Regarding the three dimensional structure of the polypeptide of SEQ ID NO: 2, it is true that there is no requirement for said structure, but there is an enablement requirement as indicated above. While the high throughput screening methods are known in the art and have some success in obtaining variants with specific characteristics, the amount of experimentation is enormous, and expectation of obtaining a specific 6-desaturation activity would be doubted by one of ordinary skill in the art. Finally with regard to the Board of Patent Appeal and Interference decision, Appeal No. 2004-2319 in application 09/915,694, the scope of the claims is considered reasonable by the examiner. It should be noted that claims directed to 95% sequence homology are not included in this rejection.

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 298, 299, 301-309, 330, 343, 356, and 369 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) The clause "that hybridizes preferentially to the complement of the sequence depicted in SEQ ID NO: 1 under hybridization conditions suitable for selectively screening a recombinant DNA library" in claim 298 renders the claims indefinite and confusing. The conditions are not identified by the specification, and one of ordinary skill in the art would not know what the applicant have used. This rejection is made against canceled claims 275 and 279 in the previous Office action. For examination purposes only, the phrase is taken to mean any hybridization conditions.

In response to the above rejection, applicants argue that the rejection is moot due to cancellation of claim 275 and 297, and provide no new arguments.

(b) Claims 299, 301-309, 330, 343, 356, and 369 are included with these rejections because they are dependent on a rejected claims and do not cure its deficiencies.

Claims 323, 324, 336, 337, 349, 350, 362, 363, and 373 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Claims 215-224, 255-264, 325, 328, 338, 341, 351, 354, 364, and 367 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTWTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr, Ph. D. can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nashaat T. Nashed, Ph. D.
Primary Examiner
Art Unit 1652